Outcome after Functional Hemispherectomy in Children with Rasmussen Encephalitis: A Report of 20 Years' Experience at King Chulalongkorn Memorial Hospital

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Background: Rasmussen's encephalitis (RE) is characterized by unilateral cerebral inflammation of the cerebral cortex and drugresistant epilepsy. Functional hemispherectomy (FH) remains the only effective cure. There is no prior Thai children-case-report.

Objective: To review King Chulalongkorn Memorial Hospital (KCMH) pediatric clinical, magnetic resonance imaging (MRI), and treatment-outcome of RE.

Materials and Methods: This report is a retrospective review of pediatric RE treated with FH. The authors described twentyyear of experience and outcome after FH with three years follow-up at KCMH. Demographic, clinical data, seizures duration, electroencephalogram (EEG), and neuroimaging before FH were collected. Seizure frequency and functional deficit after FH were collected. All RE patients diagnosed by criteria of the European consensus criteria.

Results: Seven patients were diagnosed with RE and had FH. The mean epilepsy-onset age was 73.29±31.39 months, mean diagnosis-age was 91.43±31.15 months, and mean surgery-age was 95.57±31.89 months. Duration between seizure-onset to surgery was 21.29±12.05 months. All EEG showed focal seizures at the right-hemisphere 3 from 7 (42.9%). At the time of surgery, patients had right-hemiparesis 5 from 7 (71.4%) and epilepsia partialis continua (EPC) 4 from 7 (57.1%). Comorbid diseases were attention deficit hyperactivity disorder (ADHD), tics, learning disability, and possible systemic lupus erythematosus (SLE). MRI showed caudate atrophy 3 from 7 (42.9%), T2-hyperintensity 5 from 7 (71.4%), progressive atrophy 4 from 7 (57.1%), and cerebral-hemisphere atrophy 6 from 7 (85.7%). All patients had regression in activity of daily living (ADL), school performance, and quality of life. Outcome after FH were seizure-reduction in 99.44% (95% CI –109.68 to –75.1, p=0.018) and antiepileptic drug (AED) decrease (95% CI 0.61 to 3.1, p=0.047). Regression stopped with better ADL and decrease in seizure-frequency with no worsening of seizure.

Conclusion: RE should be planned in focal intractable epilepsy with EPC and progressive hemiparesis. Appropriate surgical treatment such as FH improves clinical seizures, quality of life, and stop clinical regression.

Keywords: Pediatric, Rasmussen encephalitis, Hemispherectomy, Magnetic resonance imaging (MRI), Outcome, Quality of life

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Rasmussen encephalitis (RE) is a unilateral chronic inflammation of the cerebral cortex. It was first described by a neurosurgeon Rasmussen et al in 1958⁽¹⁾. Clinical features are focal epilepsy with

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multiple drugs resistant, progressive hemisphere cerebral atrophy, and cognitive deterioration. It is found in pediatric patients less than 10 years old, with a mean age of six years old, and it is less common in adult⁽²⁾. RE is a rare condition. The incidence is at one case per 500,000 to 1,000,000 people per year^(3,4).

The 2005 European consensus^(2,5,6) on pathogenesis, diagnosis, and treatment of Rasmussen's encephalitis remains the accepted guideline for evaluative criteria. The primary cause remains unknown. Neuropathological and immunological studies support the notion that Rasmussen's

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encephalitis is probably driven by humoral and T-cell response⁽⁶⁾. Diagnosis contributes to clinical feature of focal seizure, hemiparesis, neuroimaging, and histopathology. There is no specific investigation for RE. Treatment with anti-epileptic drug (AED), intravenous immunoglobulin (IVIG), plasmapheresis, and immunosuppressive drug temporary relieve. Functional cerebral hemispherectomy (FH) remains the only cure for seizures, but there are inevitable functional compromises. Outcome of early surgery protects the contralateral normal hemisphere from repeated seizures and progressive neuropsychological loss.

In Thailand, there has been no prior report case series. The authors described twenty years' experience of Rasmussen's encephalitis in seven children and the outcome after FH with three years follow-up at King Chulalongkorn Memorial Hospital.

Materials and Methods

A retrospective chart review was performed in children who had clinical course and neuroradiological feature typical of RE and were treated with FH between March 1, 1997 and March 1, 2017. Data collected were demographic data, clinical and duration of seizures, electroencephalogram (EEG), and neuroimaging data prior to functional hemispherectomy. The outcome after surgery including seizure frequency, quality of life, and functional deficit were collected.

Quality of life was evaluated by the Thai version of the Quality of Life in Epilepsy Inventory for Adolescents (QOLIE-AD-48) with permission from Phonwisuth et al, Department of Pediatrics, Ramathibodi Hospital⁽⁷⁾.

Statistical analysis

The quantitative data was summarized as percentages, median, range, and mean \pm standard deviation (SD). Wilcoxon signed ranks test was used to compare two related samples such as the reduction of seizure after surgery and number of AED after surgery. A p-value of 0.05 or less was considered as significant. Statistics was analyzed by IBM SPSS Statistics software, version 22 (IBM Corp., Armonk, NY, USA).

Results

Eight patients were diagnosed with Rasmussen's encephalitis and were treated with functional hemispherectomy. There were four males and four females with a mean age at epilepsy onset of five years five months (range three years eight months to ten years old, 73.25 ± 29.56 months). The mean age at diagnosis was seven years ten months (range four years nine months to thirteen years three months old, 99.88 ± 37.45 months). The mean age at surgery was eight years two months (range four years ten months to thirteen years hour months old, 103.63 ± 37.29 months). Duration between onset of seizure to surgery was two years one month (range two months to seven years four months, 29.63 ± 26.09 months). EEG showed focal seizures on the right side in three from the eight patients (37.5%). At the time of surgery all patients had hemiparesis. Five out of eight patients had right hemiparesis (62.5%) and only four out of eight patients developed epilepsia partialis continua (EPC, 50%) (Table 1).

All of the patients were diagnosed by criteria of the European consensus criteria part A (Table 2) and had regression such as impairment of activity in daily living, school performance, and quality of life from seizure. Comorbid diseases such as fungal tracheitis, attention deficit hyperactivity disorder (ADHD), tics, learning disability, and possible systemic lupus erythematosus (SLE) were found. All of the patients were diagnosed with intractable focal seizure and one of the patients was on a ketogenic diet to control seizure before the surgery (Table 3). None of the patients received IVIG or immunosuppressive drugs. Magnetic resonance imaging (MRI) of four out of eight patients (50%) revealed caudate atrophy, six out of eight patients (75%) had hypersignal intensity in T2, four out of eight patients (50%) had progressive atrophy after surgery, and seven out of eight patients (87.5%) had cerebral hemispheric atrophy ipsilateral. In the sixth patient, whose duration between onsets of seizure to surgery was 44 months, MRI showed multiple cerebral atrophy bilateral hemisphere. EEG, clinical, and ictal single photon emission computed tomography (SPECT) were concordant with the left RE. In the eighth patient whose delayed FH until 88 months (seven years four months) after seizure onsets, the outcome was unchanged in the number of seizures, increased the number of AED required the patient to remain bedridden, and required tracheostomy.

All the patients had cerebral functional hemispherectomy while the pathology revealed typical RE in five out of eight patients. The outcome after functional hemispherectomy revealed that all the seizure stopped immediately in two out of eight patients, reduced seizure frequency in five out of eight patients, and no change in seizure frequency in one out of eight patients. Outcome after surgery can be collected in only seven patients. There was no seizure

| Table 1. Patient demographics data and seizure character- |
|-----------------------------------------------------------|
| istic |

| | n (%) |
|-------------------------------------------|----------------------|
| Number of patients | 8 (100) |
| Sex | 0(100) |
| Female | 4 (50.0) |
| Male | 4 (50.0) |
| Age at onset (months); mean±SD | 73.25±29.56 |
| Median (min, max) | 65 (44, 120) |
| Age at diagnosis (months); mean±SD | 99.88±37.45 |
| Median (min, max) | 94 (57, 159) |
| Age at surgery (months); mean±SD | 103.63±37.29 |
| Median (min, max) | 98.5 (58, 160) |
| Duration before surgery (months); mean±SD | 29.63±26.09 |
| Median (min, max) | 25 (2, 88) |
| Seizure characteristic | 23 (2,00) |
| Focal seizure right/left side (EEG) | |
| Left side | 5 (62.5) |
| Right side | 3 (37.5) |
| EPC | 5 (57.5) |
| • No | 4 (50.0) |
| • Yes | 4 (50.0) |
| Hemiparesis right/left side | 4 (50.0) |
| Left side | 3 (37.5) |
| Right side | 5 (62.5) |
| Comorbid disease | 3 (02.3) |
| ADHD | 1 (12.5) |
| ADHD, LD, tics | 1 (12.5) |
| None | 4 (50.0) |
| Possible SLE | 1 (12.5) |
| Tracheitis | 1 (12.5) |
| No. of AED before surgery; mean±SD | 3±1 |
| Median (min, max) | 3 (2, 4) |
| Other seizure treatment | 0 (2, 1) |
| KD | 1 (12.5) |
| None | 7 (87.5) |
| MRI characteristic | , (07.5) |
| Caudate atrophy (yes) | 4 (50.0) |
| Hypersignal T2 (yes) | 4 (30.0) 6 (75.0) |
| Progressive atrophy (yes) | 4 (50.0) |
| Hemisphere atrophy (yes) | 7 (87.5) |
| Tempphere actopity (yes) | , (07.5) |

SD=standard deviation; EEG=electroencephalogram; EPC=epilepsia partialis continua; ADHD=attention deficit hyperactivity disorder; LD=learning disability; SLE=systemic lupus erythematosus; AED= antiepileptic drug; KD=ketogenic diet; MRI=magnetic resonance imaging

data of the eighth patient because he could not come for follow-up. The seizure frequency after surgery dropped by 99.44% (p=0.018) at three years followup. It also decreased the required AED number from 3 to 2 AED (p=0.047). At three years after surgery, two patients did not require anticonvulsant and four patients had decreased AED number and doses. Two patients had increased the AED numbers and doses after surgery.

After surgery, the parents reported that clinical regression stopped. One patient was well for school performance. He could perform activity of daily living and was seizure free. Five patients had reported improvement in daily living but were unable to attend school and the seizure was reported to have decreased. One patient had no clinical improvement. The eighth patient had no result due to lost follow-up.

The quality of life was evaluated by the Thai version of the QOLIE-AD-48, with permission from Phonwisuth et al, Department of Pediatrics, Ramathibodi Hospital⁽⁷⁾. The questionnaires were answered by only three patients. Because the patients were not able to answer the questionnaires by themselves, the authors had their parents answer the questionnaires for them. The result found that eight domains from 48 items consisted of epilepsy impact, memory-concentration, attitude, physical function, stigma, social support, school behavior, and health perceptions. The questionnaires were scored to T-scores. Each subscale and the total (summary) score were determined. Higher T-scores reflect a more favorable quality of life.

Only three patients responded to the questionnaire (QOLIE-AD-48). The mean total score and SD of QOLIE-AD-48 of RE patients in the present study were 39.42 and 6.10, respectively (Table 4). The lowest score was in the domain of school behavior and the highest score was in the domain of health perception (Table 5). All of the domains of QOILE were lower than 50% from the T-score reflecting low quality of life.

Discussion

RE is a unilateral chronic inflammation of cerebral cortex. To improve the authors understanding of the RE in Thai children, the authors carefully reviewed the long-term outcomes of eight pediatric epilepsy cases that underwent FH at the authors hospital. The average age of onset was the same as in previous studies⁽⁸⁻¹⁰⁾. The average duration between onset of seizure to surgery was two years one month, which was less than previous studies^(9,10). All patients had drug resistant focal seizures or hemiparesis. EPC presented in only 50%, which is in the lower range

| Part A: | | Clinical: Focal se EG: Unihemisp MRI: Unihemisp Grey or white Hyperintense H Clinical: Epileps MRI: Progressiv | Clinical: Focal seizures (with or without epilepsia partialis continua) and unilateral cortical deficit(s) EEG: Unihemispheric slowing with or without epileptiform activity and unilateral onset MRI: Unihemispheric focal cortical atrophy and at least one of the following Grey or white matter T2/FLAIR hyperintense signal Hyperintense signal or atrophy of the ipsilateral cudate head I. Clinical: Epilepsial partialis continua or progressive* unilateral cortical deficit(s) MRI: Progressive* unihemispheric focal cortical atrophy J. Elifopathology: T-cell dominated encephalitis with activated microglial cells (typically, but not necessarily forming n. Numerous parenchymal macrophages, B cells or plasma cells or viral inclusion bodies exclude the diagnosis of RE | hout epilepsia parti or without epileptii atrophy and at leas hyperintense signal of the ipsilateral cat a or progressive* u focal cortical atroph ncephalitis with act nhages, B cells or pli ance imaging; CT=c inical examinations me. To indicate prog | psia partialis continua) and ur tepileptiform activity and unil at at least one of the following use signal ateral caudate head essive* unilateral cortical defi essive* unilateral cortical defi at atrophy s with activated microglial cell ells or plasma cells or viral inc ing: CT=computed tomography ing: CT=computed tomography inctions or MRI studies are re cate progressive hemiatrophy KE patients before surgery | if ollowin ur, followin ur, followin ur, followin urtical de orglial ce or viral it ornograp dies are dies are miatroph | nilatera liateral ficit(s) fis (typi hy; EEG hy; each ty, each | l onset l onset noset n bodies excl 3-electroenc ed to meet th i of these MR | leficit(s) ot necessarily for clude the diagnosi cephalogram; FLA he respective crite RIs must show her | ming nodu s of RE ria. To ind- eria. To ind- miatrophy. | Part A: 1. Clinical: Focal seizures (with or without epilepsia partialis continua) and unilateral cortical deficit(s) 2. EEG: Unihemispheric focal cortical atrophy and ta least one of the following 3. MRI: Unihemispheric focal cortical atrophy and at least one of the following Grey or white matter TZ/FLAIR hyperimense signal Hyperimtense signal or atrophy of the ipsilateral cudate head Bart B: 1. Clinical: Epilepsial partialis continua or progressive* unilateral cortical deficit(s) 2. MRI: Progressive* unihemispheric focal cortical atrophy 2. MRI: Progressive* unihemispheric focal cortical atrophy 2. MRI: Progressive* unihemispheric focal cortical atrophy 3. MRI: Progressive* unihemispheric focal cortical atrophy 4. Histopathology: T-cell dominated encephalitis with activate direction bodies exclude the diagnosis of RE Numerous parenchymal macrophages. B cells or plasma cells or viral inclusion bodies exclude the diagnosis of RE RF-hasmusen encephalitis, MRI-magnetic resonance imaging. CT-computed tomography: EEG-electronencephalogram; FLAR=fluid-attenated inversion recovery *Progressive means that at least two sequential clinical examinations or MRI studies are required to meet the respective criteria. To indicate clinical progressive, each of these examinations must document a neuclogical defict, and this must increase over time. To indicate progressive hemistrophy, and this must increase over time. Table 3. Clinical and demographic characteristics of RE patients before surgety | gliosis covery ve, each of the e over time. | ise examinat | ions must doc | ument a |
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| | ŝ | L. Clinical: Epileps 2. MRI: Progressiv | ial partialis continu e* unihemispheric f T-cell dominated ei arenchymal macrop | a or progressive* u focal cortical atroph ncephalitis with act hages, B cells or pla ance imaging, CT=c inical examinations me. To indicate prog | y y ivated mic sma cells (or MRI stu ressive he ressive he ressive he | rttical de roglial ce or viral ir omograpi dies are miatroph | ficit(s) ills (typi hy; EEG hy; EEG iy, each y | n bodies excl n bodies excl 3=electroenc ed to meet th of these MR | ot necessarily forr Jude the diagnosi: cephalogram; FLA he respective crite RIs must show her | ming nodu s of RE JR=fluid-a eria. To ind miatrophy | les) and reactive astrc tenuated inversion re icate clinical progress and this must increas | gliosis covery ve, each of the s over time. | ise examinati | ions must doc | ument a |
| Part B: | | Histopathology: - Numerous pe | | ance imaging; CT=c [,] inical examinations ne. To indicate prog | imputed tr or MRI stu ressive hei nts befor | mograpl dies are miatroph e surger | hy; EEG required y, each y | i=ele ctroenc | cephalogram; FLA he respective crite XIs must show her | JR=fluid-a sria. To ind miatrophy, | ttenuated inversion re icate clinical progress! and this must increas | covery ve, each of the over time. | se examinati | ions must doc | ument a |
| * Prog neurol Table | ressive 1 logical d | means that at least leficit, and this muticity and this muticity and this muticity and the second se | * Progressive means that at least two sequential clinical examineurological deficit, and this must increase over time. To indi To indi Table 3. Clinical and demographic characteristics of I | istics of RE patie | | | 2 | | | | | | | | |
| Patient | Sex | Age at onset | Age at diagnosis | Age at surgery | _ | | EPC Her | Hemiparesis | | Other | Neuroimaging before surgery | ery. | | MRI | |
| No. | | | | | before s surgery (month) (| seizure R/L (EEG) | | | disease tr | treatment – | MRI CT | Caudate atrophy | Hypersignal T2 | Progressive atrophy | Hemisphere atrophy |
| 1 | Male | 3 years 8 months | 4 years 9 months | 4 years 10 months | 14 | Left Y | Yes | Right | ADHD, LD, tics | No | 2 0 | No | Yes | Yes | Yes |
| 2 | Female | e 4 years 6 months | 6 years 3 months | 6 years 9 months | 27 | Right N | No | Right | None | No | 1 1 | No | No | Yes | Yes |
| 33 | Female | 4 years | 5 years 3 months | 5 years 11 months | 23 | Left N | No | Right | Possible SLE | No | 2 0 | Yes | Yes | Yes | Yes |
| 4 | Male | 9 years 9 months | 9 years 10 months | 9 years 10 months | 2 | Left Y | Yes | Right | ADHD | KD | 2 1 | Yes | Yes | No | Yes |
| ъ | Female | 5 years 2 months | 6 years 5 months | 6 years 6 months | 16 | Right Y | Yes | Left | None | No | 2 0 | No | Yes | No | Yes |
| 9 | Female | 5 years 8 months | 9 years 3 months | 9 years 8 months | 44 | Left Y | Yes | Right | None | No | 3 0 | No | Yes | Yes | No |
| 7 | Male | 10 years | 11 years 7 months | 12 years 3 months | 27 | Right N | No | Left | None | No | 1 1 | Yes | No | No | Yes |
| 8 | Male | 6 years 1 months | 13 years 3 months | 13 years 4 months | 88 | Left N | No | Left F | Fungal tracheitis | No | 1 0 | Yes | Yes | No | Yes |

Table 2. Diagnostic criteria for Rasmussen encephalitis⁽²⁾

Table 4. Quality of life evaluated by Thai version of theQuality of Life in Epilepsy Inventory for Adolescents (QOLIE-AD-48)

| Subscale | | Obser | ved final | score | |
|----------------------|-------------|-------------|-------------|-------|-------|
| | PG (pt1) | PK (pt2) | SP (pt3) | Mean | SD |
| Epilepsy impact | 58.33 | 25 | 25 | 36.11 | 19.24 |
| Memory-concentration | 37.5 | 35 | 65 | 45.83 | 16.65 |
| Attitude | 27.075 | 22.92 | 0 | 16.67 | 14.58 |
| Physical function | 50 | 35 | 55 | 46.67 | 10.41 |
| Stigma | 34.71 | 37.5 | 30.55 | 34.25 | 3.50 |
| Social support | 68.75 | 43.75 | 25 | 45.83 | 21.95 |
| School behavior | 62.5 | 25 | 56.25 | 47.92 | 20.09 |
| Health perceptions | 41.6 | 66.66 | 50 | 52.75 | 12.75 |
| Total score | 46 | 34.14 | 37.59 | 39.24 | 6.10 |

SD=standard deviation

Table 5. T-score of QOLIE-AD-48

| Subscale | | | T-score | | |
|----------------------|-------------|-------------|-------------|-------|-------|
| | PG (Pt1) | PK (Pt2) | SP (Pt3) | Mean | SD |
| Epilepsy impact | 33.04 | 45.43 | 33.04 | 37.17 | 7.15 |
| Memory-concentration | 35.44 | 36.56 | 48.83 | 40.28 | 7.43 |
| Attitude | 42.59 | 44.41 | 32.54 | 39.85 | 6.39 |
| Physical function | 40.65 | 45.55 | 47.18 | 44.46 | 3.40 |
| Stigma | 34.6 | 33.36 | 31.47 | 33.14 | 1.58 |
| Social support | 38.2 | 48.5 | 30.57 | 39.09 | 9.00 |
| School behavior | 7.59 | 31.94 | 27.88 | 22.47 | 13.05 |
| Health perceptions | 50.45 | 37.32 | 41.72 | 43.16 | 6.68 |
| Total score | 30.6 | 37.45 | 32.59 | 33.55 | 3.52 |

SD=standard deviation

when compared to previous studies. Treatments with AEDs, IVIG, plasmapheresis or immunosuppressive drug produced temporary relief in the prior reports. There was no immunotherapy or IVIG in the present study. Bien et al⁽²⁾ provided a range of 62.5% to 85% seizure freedom rate following hemispherectomy across multiple studies. The authors studied seizure freedom rate after functional hemispherectomy was markedly lower at 28.5% (2 out of 7). In the five patients who continued to have seizures, the seizure frequency was markedly lowered by 99.44%. In six out of seven patients, the number of AED was lowered by 33%. The authors overall results are still satisfactory though not as good as in prior studies (Table 6).

Two patients required higher dose of anticonvulsant after surgery (Table 3, patients No.3 and No.8). Patients No.3 had comorbidity with possible SLE and multiple AED allergies. She was ANA positive and anti-ds DNA negative during her annual follow-up of six years but did not fulfilled the criteria of SLE and did not have other organs involvement. Patient No.8 came from a highland group and could not attend the three years required follow-up. He was excluded from the surgery outcome analysis.

MRI showed hypersignal intensity at T2weighted and caudate atrophy in 75% and 50%, respectively, which is the same as the previous studies⁽¹¹⁻¹³⁾ (Table 7). Unihemispheric atrophy was found in 75% in the authors study. The sixth patient had bilateral hemispheric atrophy. Her duration between onset of seizure to surgery was the second longest at 44 months. Her seizure frequency dropped from 90 per month to seizure every two months. Progressive atrophy had only 50% due to early surgical treatment before follow-up imaging.

In previous long-term outcome studies⁽¹⁴⁻¹⁶⁾ in children who underwent functional hemispherectomy, patient with early surgical treatment had better cognitive outcome. In the authors study, all seven were able to talk and four from seven were able to attend school with special educations. No formal neuropsychological resting was performed.

Table 8 showed the QOLIE-AD-48 of the present study compared to prior studies in Thai and other countries⁽¹⁷⁻²⁰⁾. QOLIE-AD-48 revealed score lower than the previous studies in all domains, reflecting that RE patients after treatment still had significant lower quality of life than the adolescent epileptic patients.

Limitation

The present study was a small case series. Seizures were approximately reported by the parents not from seizure diary. The cognitive and language function before and after surgery were evaluated clinically only. Full neuropsychological studies were not done.

Conclusion

RE should be considered in patients who had focal seizure with EPC and progressive hemiparesis. Appropriate surgical treatment such as functional hemispherectomy improves clinical seizures and quality of life and stops cognitive regression.

What is already known on this topic?

RE in Thai children had typical clinical

| Characteristic | The present study | Hoffman, et al. (2016) ⁽⁸⁾ | Guan, et al. (2014) ⁽⁹⁾ | Granata, et al. (2014) ⁽¹⁰ |
|-------------------------|-------------------|---------------------------------------|------------------------------------|---------------------------------------|
| Number of patients | 8 | 13 | 20 | 16 |
| Male/female | 4/4 | 6/7 | 9/11 | 8/8 |
| Age at onset | 5 years 5 months | | 5.72±4.01 year | 5.8 years |
| Age at diagnosis | 7 years 10 months | 10.6 years | | |
| Age at surgery | 8 years 2 months | | 8.90±4.80 year | |
| Duration before surgery | 2 years 1 month | 5.7 years | | 3.8 years |
| Lateralization L/R | 5/3 | 8/5 | 6/14 | 4/12 |
| Focal seizure | 8 (100%) | 13 (100%) | 20 (100%) | 16 (100%) |
| EPC | 4 (50%) | 8 (62%) | 18 (90%) | |
| Hemiparesis | 8 (100%) | 8 (62%) | 18 (90%) | 16 (100%) |
| Immunotherapy | 0 (0%) | 9 (69.2%) | | 0 (0%) |
| Multiple AED | 8 (100%) | 13 (100%) | | 16 (100%) |
| Surgery | 8 (100%) | 11 (85%) | 20 (100%) | 16 (100%) |
| Seizure free | 2 (25%) | 7 (63%) | 16 (80%) | 13 (81%) |
| Seizure control | 7 (87.5%) | 13 (100%) | 19 (91%) | 16 (100%) |
| Pathology RE | 5 (62.5%) | 11 (85%) | 20 (100%) | 16 (100%) |

L/R= left/right; EPC=epilepsia partialis continua; AED=antiepileptic drug; RE=Rasmussen encephalitis

Table 7. MRI comparison to other studies

| MRI study | The present study (n=8) | Chiapparini, et al. (2003) ⁽¹¹⁾ (n=13) | Pradeep, et al. (2014) ⁽¹²⁾ (n=16) | Kuki, et al. (2018) ⁽¹³⁾ (n=23) |
|------------------------------|----------------------------|------------------------------------------------------|--------------------------------------------------|-----------------------------------------------|
| | n (%) | n (%) | n (%) | n (%) |
| Hypersignal intensity at T2W | 6 (75.0) | 12 (92.3) | 14 (87.5) | 13 (56.5) |
| Caudate atrophy | 4 (50.0) | 9 (69.2) | 6 (37.5) | 7 (30.4) |
| Unihemispheric atrophy | 7 (87.5) | 13 (100) | 16 (100) | 18 (78.2) |
| Progressive atrophy | 4 (50.0) | 13 (100) | 11 (68.7) | 18 (78.2) |

T2W=T2-weighted

Table 8. comparison between QOLIE scores across different domains and countries

| Items | The present study (n=3) | Thai, 2013 ⁽¹⁷⁾ (n=73) | US & Canada, 1999 ⁽¹⁸⁾ (n=197) | Spain, 2004 ⁽¹⁹⁾ (n=66) | China, 2010 ⁽²⁰⁾ (n=47) |
|----------------------|-------------------------|--------------------------------------|----------------------------------------------|---------------------------------------|---------------------------------------|
| | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) |
| Epilepsy impact | 36.11 (19.24) | 73.9 (23.4) | 70.6 (26.9) | 92.3 (13.8) | 70.1 (22.5) |
| Memory-concentration | 45.83 (16.65) | 60.2 (22.1) | 67.6 (22.4) | 76.0 (19.7) | 66.1 (19.8) |
| Attitude | 16.67 (14.58) | 36.7 (21.2) | 39.8 (22.8) | 35.6 (17.1) | 69.2 (22.5) |
| Physical function | 46.67 (10.41) | 59.1 (27.3) | 63.6 (30.6) | 94.8 (13.1) | 67.1 (24.7) |
| Stigma | 34.25 (3.5) | 59.6 (23.5) | 71.3 (22.0) | 86.0 (20.1) | 62.9 (26.4) |
| Social support | 45.83 (21.95) | 57.4 (25.2) | 72.4 (24.4) | 81.0 (22.3) | 33.2 (26.1) |
| School behavior | 47.92 (20.09) | 85.1 (21.3) | 90.3 (15.4) | 92.0 (18.0) | 86.3 (9.8) |
| Health perceptions | 52.75 (12.75) | 63.7 (19.0) | 65.8 (19.1) | 66.9 (14.4) | 52.8 (18.3) |
| Total score | 39.24 (6.10) | 63.9 (17.1) | 67.7 (17.3) | 80.3 (10.7) | 65.6 (14.1) |

SD=standard deviation

characteristic MRI and treatment-outcome.

What this study adds?

This study shows database of RE in Thai children for further research.

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Conflicts of interest

The authors do not report any conflict of interests concerning the materials or methods used in this study or the findings specified in this paper.

References

- Rasmussen T, Olszewski J, Lloydsmith D. Focal seizures due to chronic localized encephalitis. Neurology 1958;8:435-45.
- Bien CG, Granata T, Antozzi C, Cross JH, Dulac O, Kurthen M, et al. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: a European consensus statement. Brain 2005;128:454-71.
- Pinto D. Towards a cure for Rasmussen's encephalitis: research strategies. Gobal Genes [Internet]. 2010 [2016 Dec 26]. Available from: https://globalgenes. org/wp-content/uploads/2010/07/Overview-of-REand-Possible-Research-Directions-20101.pdf.
- Hart I. Fact sheet: Rasmussen's encephalitis [Internet]. Liverpool: The Encephalitis Society; 2010 [cited 2016 Dec 26]. Available from: https://pdfs.semanticscholar. org/c2d2/963f8ba69c2b68538186a6618c80e6feec59. pdf.
- Bien CG, Schramm J. Treatment of Rasmussen encephalitis half a century after its initial description: promising prospects and a dilemma. Epilepsy Res 2009;86:101-12.
- Varadkar S, Bien CG, Kruse CA, Jensen FE, Bauer J, Pardo CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol 2014;13:195-205.
- Phonwisuth P, Visudtibhan A, Chiemchanya S, Visudhiphan P. Thai version of the Quality of Life in Epilepsy Inventory for Adolescents (QOLIE-AD-48). Thai J Pediatr 2004;43:188-94.

- Hoffman CE, Ochi A, Snead OC 3rd, Widjaja E, Hawkins C, Tisdal M, et al. Rasmussen's encephalitis: advances in management and patient outcomes. Childs Nerv Syst 2016;32:629-40.
- Guan Y, Zhou J, Luan G, Liu X. Surgical treatment of patients with Rasmussen encephalitis. Stereotact Funct Neurosurg 2014;92:86-93.
- Granata T, Matricardi S, Ragona F, Freri E, Casazza M, Villani F, et al. Hemispherotomy in Rasmussen encephalitis: long-term outcome in an Italian series of 16 patients. Epilepsy Res 2014;108:1106-19.
- Chiapparini L, Granata T, Farina L, Ciceri E, Erbetta A, Ragona F, et al. Diagnostic imaging in 13 cases of Rasmussen's encephalitis: can early MRI suggest the diagnosis? Neuroradiology 2003;45:171-83.
- Pradeep K, Sinha S, Saini J, Mahadevan A, Arivazhagan A, Bharath RD, et al. Evolution of MRI changes in Rasmussen's encephalitis. Acta Neurol Scand 2014; 130:253-9.
- Kuki I, Matsuda K, Kubota Y, Fukuyama T, Takahashi Y, Inoue Y, et al. Functional neuroimaging in Rasmussen syndrome. Epilepsy Res 2018;140:120-7.
- Jonas R, Nguyen S, Hu B, Asarnow RF, LoPresti C, Curtiss S, et al. Cerebral hemispherectomy: hospital course, seizure, developmental, language, and motor outcomes. Neurology 2004;62:1712-21.
- Ramantani G, Kadish NE, Brandt A, Strobl K, Stathi A, Wiegand G, et al. Seizure control and developmental trajectories after hemispherotomy for refractory epilepsy in childhood and adolescence. Epilepsia 2013;54:1046-55.
- Thomas SG, Chacko AG, Thomas MM, Babu KS, Russell PS, Daniel RT. Outcomes of disconnective surgery in intractable pediatric hemispheric and subhemispheric epilepsy. Int J Pediatr 2012;2012: 527891.
- Suwannachote S, Wechapinan T, Sriudomkajorn S. Quality of life in adolescent absence epilepsy at Queen Sirikit National Institute of Child Health. J Med Assoc Thai 2014;97 Suppl 6:S120-S125.
- Cramer JA, Westbrook LE, Devinsky O, Perrine K, Glassman MB, Camfield C. Development of the quality of life in epilepsy inventory for adolescents: the QOLIE-AD-48. Epilepsia 1999;40:1114-21.
- Benavente-Aguilar I, Morales-Blánquez C, Rubio EA, Rey JM. Quality of life of adolescents suffering from epilepsy living in the community. J Paediatr Child Health 2004;40:110-3.
- Sillanpää M, Shinnar S. Long-term mortality in childhood-onset epilepsy. N Engl J Med 2010;363: 2522-9.